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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/530,794

04/08/2005

Francis Thomas Boyle

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ASTRAZENECA R&D BOSTON
35 GATEHOUSE DRIVE
WALTHAM, MA 02451-1215

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| EXAMINER |
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SZNAIDMAN, MARCOS L

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| ART UNIT | PAPER NUMBER |
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1611

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02/20/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/530,794 | Applicant(s) BOYLE ET AL. | |
| | Examiner MARCOS SZNAIDMAN | Art Unit 1611 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6, 7, 10 and 12-24 is/are pending in the application.
- 4a) Of the above claim(s) 12 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6, 7, 10, 13-19 and 21-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>2 pages/02/13/08</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to applicant's reply filed on January 11, 2008.

Status of claims

Claims 1-4, 6-7, 10 and 12-24 are pending and are the subject of this office action.

Claims 12 and 20 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 24, 2007.

Claims 1-4, 6-7, 10, 13-19 and 21-24 are presently under examination.

Priority

The present application claims priority to application No. PCT/GB03/04347 filed 10/07/2003, which claims priority to foreign application No. UNITED KINGDOM 0223854.1 filed on 10/12/2002.

Response to Arguments

This is in response to applicant's arguments, filed on January 11, 2008.

Claims rejected under 35 USC 103

Applicant's arguments, see page 6 through page 9, filed on January 11, 2008, with respect to the rejection(s) of claim(s) 1-4, 6 and 17-18 under 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made (see 35 USC 112 rejection).

Rejection under 35 USC 103 is withdrawn.

Claims rejected under 35 USC 112

Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that: "it is submitted that a skilled person would have no difficulty in using the claimed invention based upon the information disclosed in the application. The description contains extensive teachings on suitable examples of both endothelin receptor antagonists and EGFR TKIs. The description also gives guidance on suitable dosage forms and cancers where the claimed combination may be effective". Applicant is reminded that the following species are under examination: ZD4054 as the endothelin receptor antagonist, ZD1839 as the EGFR TKI, and lung cancer as the type of cancer treated by the elected species. Neither the combination of the elected species (ZD4054 and ZD1839), or any of the other non-elected species enable for the treatment of lung cancer. They might enable for the treatment of ovarian cancer, based on the reference provided (Rosano et. al., Cancer Research (2007), 67, 6351-6359), but not for lung cancer. The description, definitively gives guidance on suitable dosage forms and cancers where the combination may be effective, however

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there is no experimental data to support that the described dosages have any efficacy against lung cancer. There is no data, *in vitro* or *in vivo*, about the efficacy of treating lung cancer with the combination of the endothelin receptor antagonist ZD4054, and the EGFR TKI ZD1839. In the absence of experimental data, and since there are no precedents in the literature for the treatment of any type of lung cancer with any combination of an endothelin receptor antagonist and a EGFR TKI, the enablement rejection is maintained. Claims 1-4, 6 and 17-18, which were previously rejected under 35 USC 103, are now being incorporated in the 35 USC 112 rejection.

Rejection under 35 USC 112 is maintained.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-7, 10, 13-19 and 21-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains

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subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Claims 1-4, 6-7, 10, 13-19 and 21-24 recite a composition and a method for treating lung cancer in a warm-blooded animal, such as man, in need of such treatment, which comprises administering to said animal an effective amount of the combination of an endothelin receptor antagonist (ZD4054), and a EGFR TKI (ZD1839) . However the specification fails to disclose any data to support the fact that using this particular combination (or any combination) will result in an effective treatment of lung cancer.

There is only experimental data that demonstrates the involvement of MAPK in both ET-1 and EGF osteoblastic signaling pathways (see specification, pages 15 and 16), but no data *in vivo* or *in vitro* to support the claim that this particular combination could result in an effective treatment of lung cancer. There is also no evidence in the prior art that a combination of any endothelin antagonist in combination with an EGFR TK inhibitor will result in the effective treatment of lung cancer. To the contrary, the prior art (see Doubt et. al. Nature, (1996), 379:557-560, cited by applicant) suggests that : more details of this RTK transactivation mechanism (with endothelin receptor) are needed to clarify its role in the regulation of biological processes and the pathophysiology of diseases such as cancer (see last sentence on page 560). There is no data in the present application that helps clarify this issue, at least regarding the treatment of lung cancer.

In the absence of any examples in the instant application, the unpredictability of the art of treating cancer, and in the absence of prior art suggesting that any

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combination of an of an endothelin receptor antagonist and a EGFR TKI might be effective in treating lung cancer, one skilled in the art could not use the invention of claims 1-4, 6-7, 10, 13-19 and 21-24, without undue experimentation.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on 571 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MLS

February 12, 2008


MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600